REMARKS

Claims 1, 3, 5-8, 10, 12-21, 23 and 25-27 are pending and under consideration. With this Amendment, Applicants have canceled Claims 1, 3, 5-8, 10, 12-20, 23 and 25-27 without prejudice in order to expedite prosecution and place the claims in condition for allowance. Claim 21 has been amended and Claims 28-45 have been added. A marked-up copy of the amended claims is attached at Exhibit A. For convenience, a clean copy of the pending claims after entry of the instant amendment is attached at Exhibit B.

Applicants reserve the right to prosecute any canceled subject matter in one or more continuation, divisional or continuation-in-part applications.

I. THE AMENDMENTS OF THE CLAIMS

Claim 21 has been amended to independent form and to clarify the step of comparing amplification products from a cancerous and noncancerous sample. Support for amended Claim 21 may be found in Claim 21 and Claim 1 as originally filed.

New Claims 28-45 recite methods for identifying the presence of cancerous cells in a human sample. Claims 28-34 recite primers for practicing Claim 21. Support for Claims 28-34 may be found, for example, in Claims 1, 5 and 15-16 as originally filed. Claim 35 recites a method of Claim 21 wherein the amplification reaction is a polymerase chain reaction. Support for Claim 35 may be found, for example, in Claim 3 as originally filed. Claims 36-37 recite probes that are complementary or substantially complementary to the amplification products, and are CS12 (SEQ ID NO:6), CS1 (SEQ ID NO:7) and CS3 (SEQ ID NO:8). Support for Claims 36-37 may be found, for example, in Claims 6-7 as originally filed. Claims 38-45 recite kits for carrying out the method of Claims 21 and 28-37. Support for Claims 38-45 are fully supported, for example, by Claims 17-20 as originally filed.

As the amendments are fully supported by the specification and claims as originally filed; they do not constitute new matter. Applicants submit that the amendments place the claims in condition for allowance thereby reducing the number of issues for appeal. Entry thereof is therefore respectfully requested.

II. CLAIM REJECTIONS UNDER 35 U.S.C. §112

Claims 8-14 and 21-27 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention. The Patent and Trademark Office asserts that an essential step has been omitted from Claims 21-27. Claims 8-14, 23, 25-27 have been canceled thereby making the rejection of these claims moot.

Amended Claim 21 omits no essential steps. Amended Claim 21 recites a method of identifying the presence of cancerous cells in a human sample. This method comprises the steps of determining the quantity of mRNA that encodes a β-deletion splice variant of human telomerase (hTERT mRNA) in a sample of interest and a control sample. To determine the quantity of mRNA that encodes a β-deletion splice variant of human telomerase, the mRNA in the sample is contacted with an amplification reagent, for example with primers SYC1076 and SYC1097. Following amplification, the quantity of mRNA is determined in both the sample of interest and a control sample. Identification of cancerous cells is accomplished by comparing the quantity of mRNA that encodes a β-deletion splice variant of human telomerase in the two populations; cancerous cells having a greater quantity of mRNA that encodes a β-deletion splice variant of human telomerase than control samples. Because all steps to determine the presence of cancerous cells in a human sample are elucidated, Claim 21 is definite. Claims 28-31, 33 and 35-36 depend from amended Claim 21. Applicants therefore submit that amended Claim 21 and new Claims 28-31, 33 and 35-36 are definite.

Applicants respectfully request that the rejection of Claims 8-14, 21, 23, and 25-27 under 35 U.S.C. §112, second paragraph be withdrawn. Applicants also submit that new Claims 28-32 and 35-36 meet the requirements for patentability under 35 U.S.C. §112.

III. CLAIM REJECTIONS UNDER 35. U.S.C. §103(a)

A. REJECTION OF CLAIMS 1, 3, 5-7, 15-16 UNDER 35 U.S.C. §103(a)

Claims 1, 3, 5-7 and 15-16 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Kilian et al. (Human Molecular Genetics, Vol. 6, No. 12, pg 2011-2019, 1997) in view of Hudkins et al. (U.S. Pat 5, 475,110, December 1995) further in view of Nakamura et al. (Genbank Accession Number AF01950, August 1997, "Nakamura 1").

Claims 1, 3, 5-7 and 15-16 have been canceled thereby rendering the rejection of these claims moot. Applicants respectfully request that the rejection of Claims 1, 3, 5-7 and 15-16 under 35 U.S.C. §103(a) be withdrawn.

B. REJECTION OF CLAIMS 21, 23, 25-27 UNDER 35 U.S.C. §103(a)

Claims 21, 23 and 25-27 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Kilian in view of Hudkins, in view of Nakamura 1 as applied to Claims 1, 3, 5-7 15 and 16 and further in view of Nakamura (Science, Vol 277, pg 955-959, August 1997, "Nakamura 2").

Claims 23 and 25-27 have been canceled thereby rendering the rejection of these claims moot.

Amended Claim 21 recites a method of identifying the presence of cancerous cells in a human sample. The method comprises determining the quantity of mRNA that encodes a β-deletion splice variant of human telomerase in a sample of interest and a control sample. According to the invention, a β-deletion splice variant of human telomerase provides an accurate measure of telomerase activity and an accurate indication of the presence of cancerous cells. Claims 28-31, 33 and 35-36 depend from amended Claim 21.

Kilian does not teach a method of identifying the presence of cancerous cells from the quantity of mRNA that encodes for a β-deletion splice variant of human telomerase in a sample. Kilian teaches that a number of human telomerase catalytic subunit 1 (hTCS1) variants encode truncated proteins, including a β-deletion. But Kilian does not teach or suggest the association between a β-deletion and telomerase activity or cancerous cells. While the detection of variant hTCS1 transcripts was a prominent feature of the Kilian analysis, Kilian was unaware of the function of these variants. ("A full understanding of the significance of these variants awaits characterization of the functional properties of all the protein derivative and direct assessment of proteins produced in various cell types." p. 2016, col 1).

Hudkins cannot cure the deficiency of Kilian because Hudkins does not teach or suggest an association between a β-deletion and telomerase activity or cancerous cells. Hudkins teaches the synthesis and use of fused purrolocarbazoles. A description of the analysis and quantification of indoleamine 2,3-dioxygenase ("IDO") mRNA is provided at Column 19, lines 34-56. Hudkins also does not teach the identification of cancerous cells by

quantitation of mRNA that encodes a β-deletion splice variant of human telomerase. Thus, Hudkins does not teach each and every element of the claimed subject matter.

Nakamura 1 also does not teach the association between a β-deletion and telomerase activity or cancerous cells. Nakamura 1, a Genbank Accession Number reference, merely teaches the nucleic acid sequence of the hTERT gene encoding sequence and no more. The nucleic acid sequence does not teach telomerase splice variants or the association of any splice variant, such as a β-deletion, with cancerous cells. Thus, Nakamura 1 does not teach each and every element of the claimed subject matter.

Nakamura 2 also does not teach the association between a β-deletion and telomerase activity or cancerous cells. Nakamura 2 instead teaches the disparity between human telomerase reverse transcriptase quantities in normal cells and cancerous cells. Nakamura 2 does not teach human telomerase splice variants such as a β-deletion or any association of such variants with cancerous cells.

Thus, Kilian, Hudkins, Nakamura 1 and Nakamura 2 alone or in any combination do not teach the association between the β-deletion and telomerase activity or cancerous cells. Therefore, the references do not teach each and every element of Claims 21 and 28-45. Applicants respectfully request that the rejection of Claim 21 under 35 U.S.C §103(a) be withdrawn. Applicants also submit that new Claims 28-45 meet the requirements for patentability under 35 U.S.C §103(a).

C. REJECTION OF CLAIMS 1, 3, 5-8, 10, 12-14, 21, 23, 25-27 UNDER 35 U.S.C. §103(a)

Claims 1, 3, 5-8, 10, 12-14, 21, 23 and 25-27 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kilian in view of Hisatomi et al (International J. Oncology, Vol 14, pg 727-732, 1999) further in view of Nakamura 1.

Claims 1, 3, 5-8, 10, 12-14, 23 and 25-27 have been canceled thereby making the rejection of these claims moot. Applicants respectfully request that the rejection of Claims 1, 3, 5-8, 10, 12-14, 21, 23 and 25-27 under 35 U.S.C. §103(a) be withdrawn.

Amended Claim 21 and Claims 28-45 recite a method as provided in section I and II, above. Kilian and Nakamura 1 do not teach or suggest an association between a β-deletion and telomerase activity or cancerous cells as discussed in section III A and III B, above.

Hisatomi does not teach or suggest any association between a β-deletion and telomerase activity or cancerous cells. Hisatomi teaches an association between levels of human telomerase reverse transcriptase (hTERT) mRNA and telomerase activity in hepatocellular carcinoma. However, Hisatomi does not teach or suggest splice variants of human telomerase, such as a β-deletion or an association of such variants with cancerous cells.

Thus, Kilian, Hisatomi and Nakamura 1 alone or in any combination do not teach or suggest an association between a β-deletion and telomerase activity or the presence of cancerous cells. Therefore, the references do not teach each and every element of Claim 21 and Claims 28-45. Applicants respectfully request that the rejection to Claim 21 under 35 U.S.C §103(a) be withdrawn. Applicants also submit that new Claims 28-31 meet the requirements for patentability under 35 U.S.C §103(a).

D. REJECTION OF CLAIMS 1, 3, 5-7, 21, 23, 25-27 UNDER 35 U.S.C. §103(a)

Claims 1, 3, 5-7, 21, 23, 25-27 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kilian in view of Meyerson et al (Cell, Vol 90, pg 785-795, August 1997) further in view of Nakamura 1.

Claims 1, 3, 5-7, 23 and 25-27 have been canceled thereby making the rejection of these claims moot. Applicants respectfully request that the rejection of Claims 1, 3, 5-7, 23 and 25-27 under 35 U.S.C. §103(a) be withdrawn.

Amended Claim 21 and Claims 28-45 recite a method as provided in section I and II, above. Kilian and Nakamura 1 do not teach or suggest the association between a β-deletion and telomerase activity or the presence of cancerous cells as discussed in section III A and III B, above.

Meyerson also does not teach the association between the β-deletion and telomerase activity or the presence of cancerous cells. Meyerson teaches cloning of the gene encoding the catalytic subunit of telomerase. Meyerson teaches a greater expression of telomerase in cancerous cells than in noncancerous cells. Meyerson does not teach splice variants, such as a β-deletion or an association of such variants with cancerous cells.

Thus, Kilian, Nakamura 1 and Meyerson alone or in any combination do not teach or suggest the association between a β-deletion and telomerase activity or the presence of cancerous cells. Therefore, the references do not teach each and every element of Claim 21

and Claims 28-45. Applicants respectfully request that the rejection to Claim 21 under 35 U.S.C §103(a) be withdrawn. Applicants also submit that new claims 28-45 meet the requirements for patentability under 35 U.S.C §103(a).

E. REJECTION OF CLAIMS 17-20 UNDER 35 U.S.C. §103(a)

Claims 17-20 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kilian in view of Hudkins as applied to Claims 1, 3, 5-7, 15-16 above, in view of Nakamura 1 in further view of Stratagene Catalog (1988).

Claims 17-20 have been canceled thereby rendering the rejection of these claims moot.

New Claims 38-45 recite kits to identify cancerous cells. The kits include instructions for identifying the presence of cancerous cells. Neither Kilian, Hudkins nor Nakamura 1 teach or suggest the association between a β-deletion and telomerase activity or the presence of cancerous cells as described in Section II and III B, above.

Stratagene does not teach or suggest the association between a β-deletion and telomerase activity or the presence of cancerous cells. The Stratagene Catalog merely shows that reagents needed for molecular biology research may be packaged in kits. Thus, the Stratagene Catalog does not relate to the claimed subject matter.

Thus, Kilian, Hudkins, Nakamura 1 and Stratagene alone or in any combination do not teach or suggest the association between a β-deletion and telomerase activity or the presence of cancerous cells. Therefore, the references do not teach each and every element of Claim 21 and Claims 28-45. Applicants respectfully request that the rejection to Claim 21 under 35 U.S.C §103(a) be withdrawn. Applicants also submit that new Claims 28-45 meet the requirements for patentability under 35 U.S.C §103(a).

CONCLUSION

Applicants submit that Claims 21 and 28-45 satisfy all the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly solicited.

No fee in addition to the fees for extension of time and notice of appeal is believed due in connection with this response. However, pursuant to 37 C.F.R. §1.136 (a)(3), the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. §1.17 and all

required extension of time fees, or credit any overpayment, to Pennie & Edmonds U.S. Deposit Account No. 16-1150. A copy of this sheet is enclosed for accounting purposes.

Respectfully submitted,

Date: December 20, 2001

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Exhibit A

Claim Amendments: Marked up Copy

21. (Amended) A method for identifying the presence of cancerous cells in a human sample wherein said method comprises:

(a) determining the quantity of [quantitating] hTERT mRNA in said sample and in a control sample of non cancerous cells by: [using the method of Claim 1; and]

(1) contacting RNA from said sample and said control sample with a pair of primers, wherein said pair of primers consists of a first primer capable of hybridizing within exon 8 or downstream of exon 8 of the hTERT gene and a second primer capable of hybridizing upstream of exon 8 of the hTERT gene;

(2) amplifying the nucleic acid sequence;

(3) measuring the generation of amplification products;

(4) determining the quantity of hTERT mRNA in said sample from the results obtained in step (3); and

(b) identifying [if] the presence of cancerous cells in said sample if the quantity of hTERT mRNA in said sample is greater than the quantity of hTERT mRNA in said control sample [are present in said sample from the quantitative result obtained in step (a)].